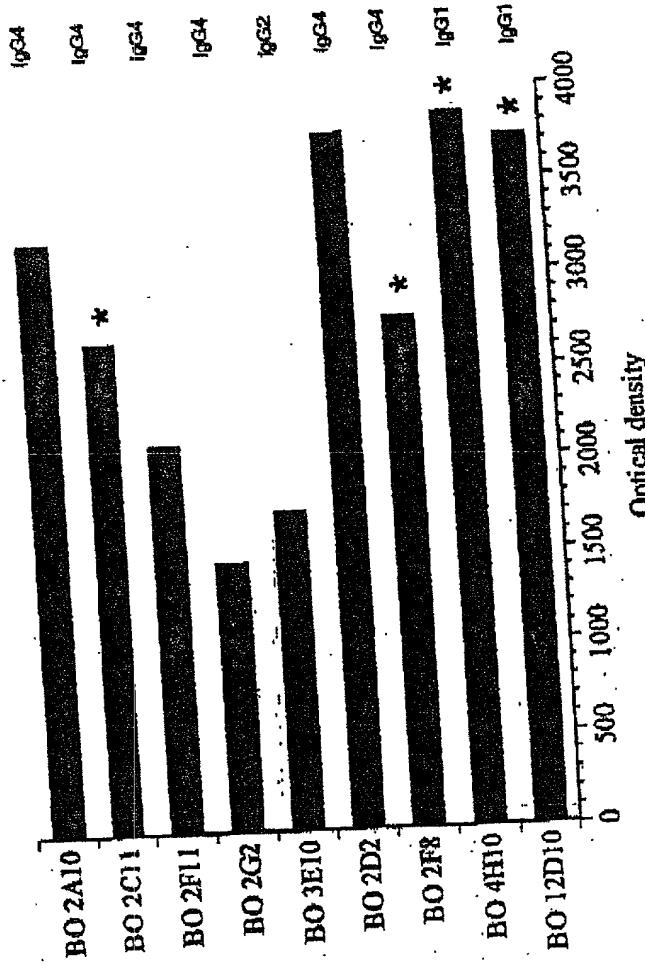


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IgG antibody binding to FVIII in ELISA



* Inhibition of FVIII activity in coagulation assay

Fig. 1

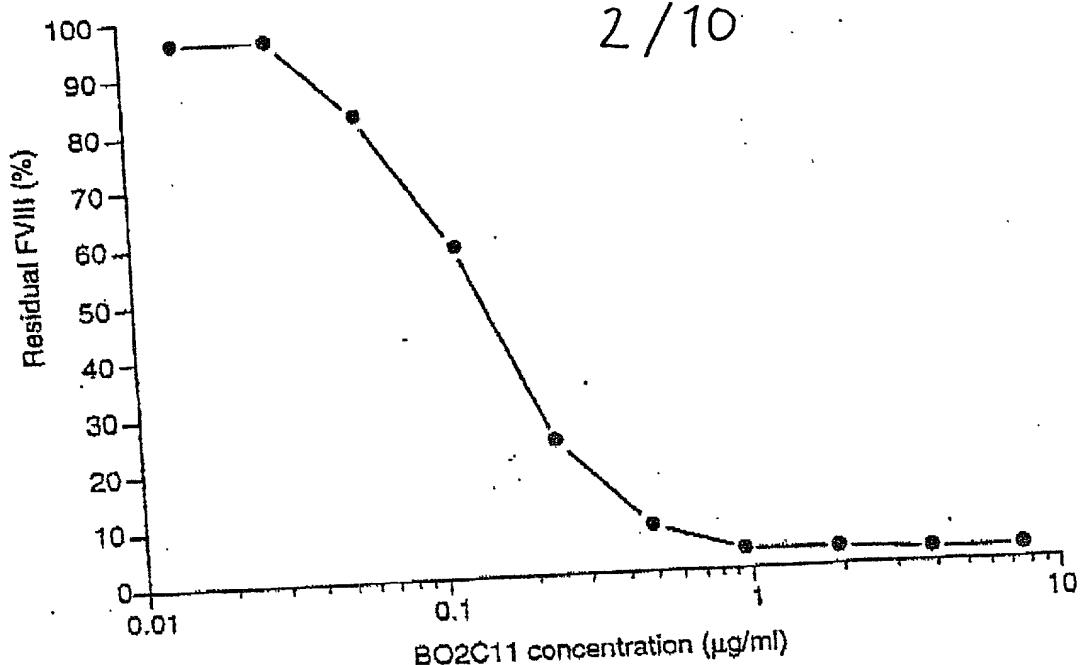


Fig. 2

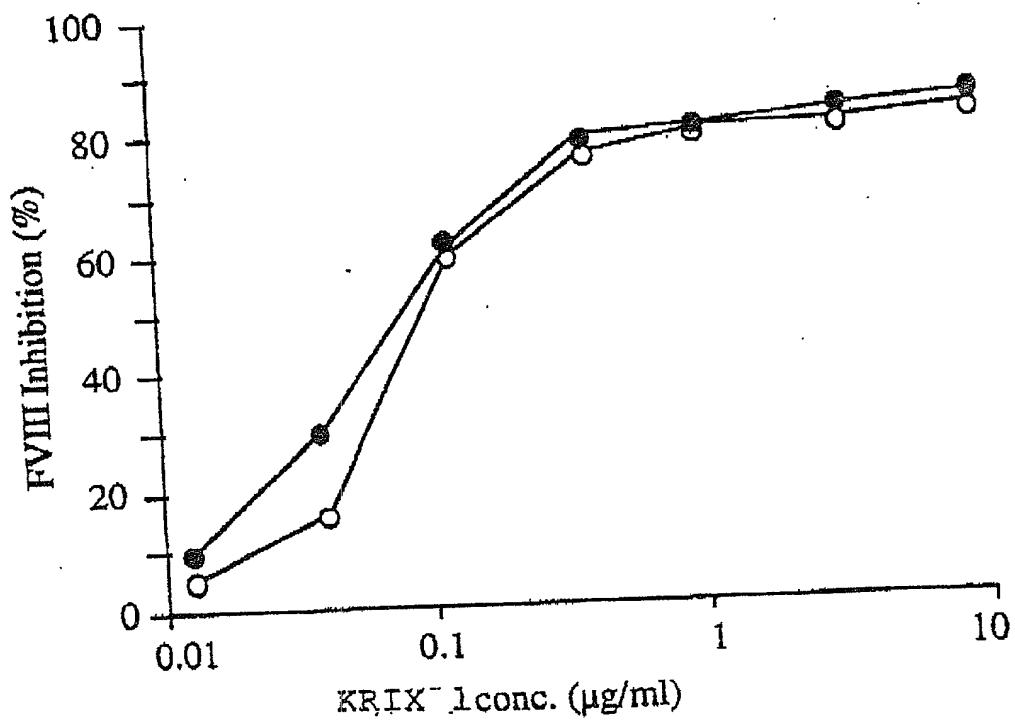


Fig. 3

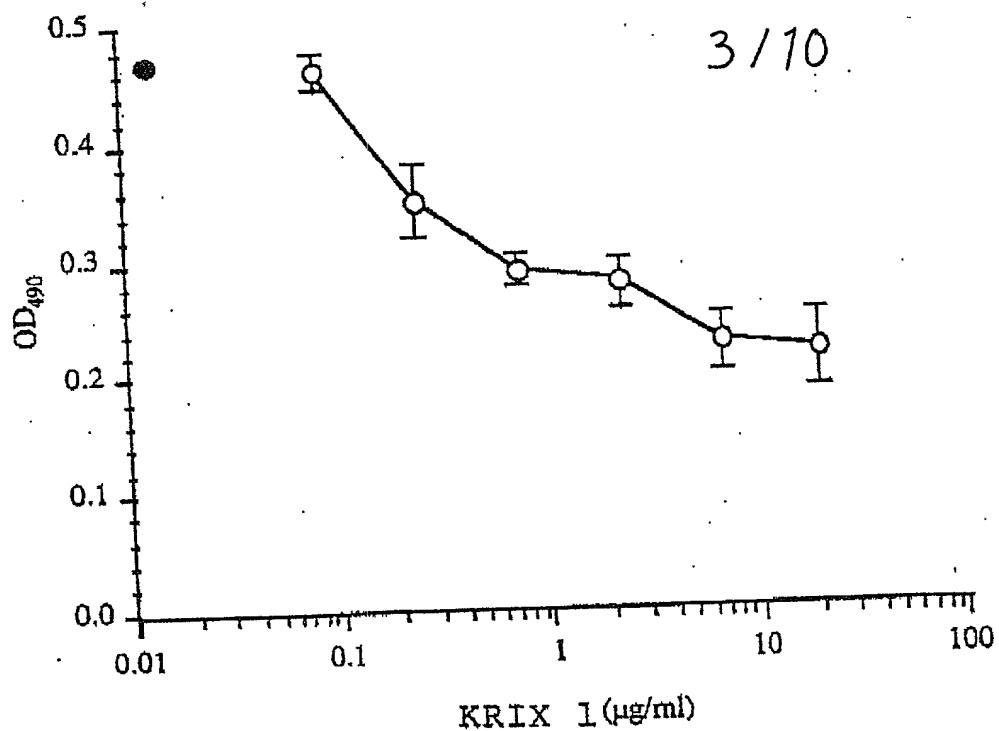


Fig. 4

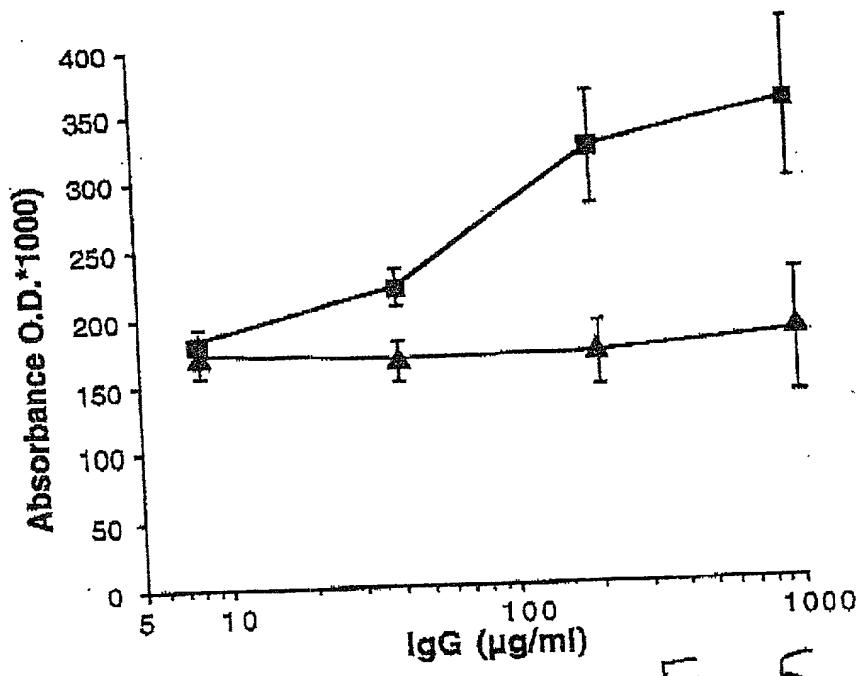


Fig. 5

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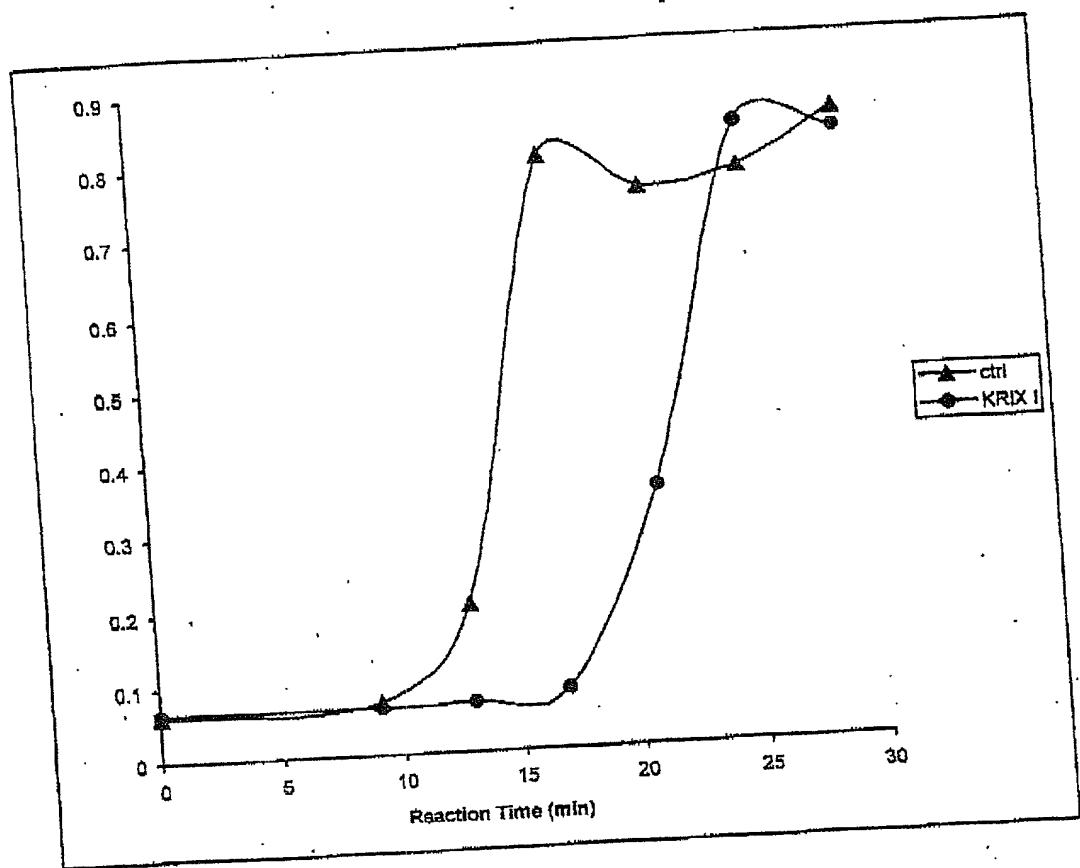


Fig. 6

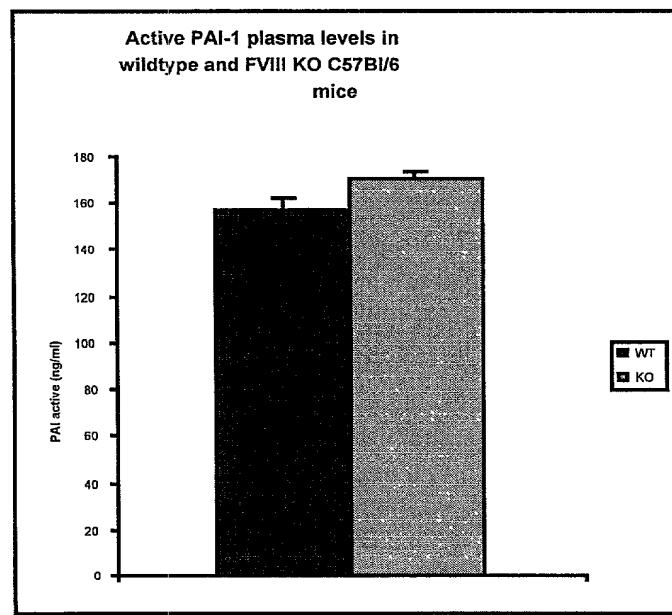
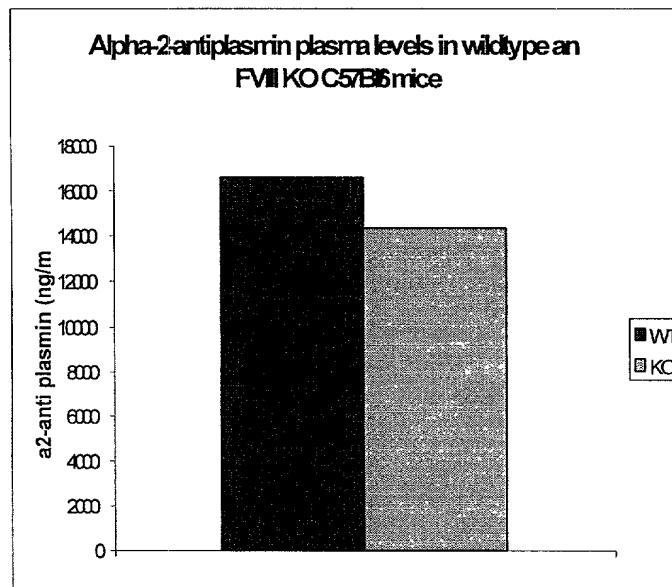
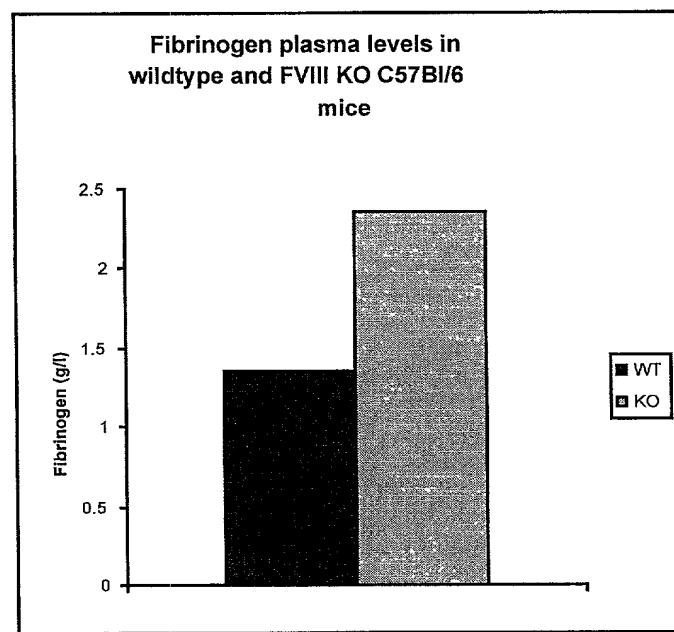
Figure 7Figure 8

Figure 9

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VH BO 2C11

1 60
atg gac tgg acc tgg agg atc ctc ttc ttg gtg gca gca gct aca ggc acc cac gcc cag
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly Thr His Ala Gln
1 20

61 120
gtc caa ctg gta cag tct ggg gct gag gtg aag aag cct ggg gcc tca gtg aag gtc tcc
Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
21 40

121 180
tgc aag gtt tcc gga tac acc ctc act gaa tta ccc gtg cac tgg gtc gga cag gct cct
Cys Lys Val Ser Gly Tyr Thr Leu Thr Glu Leu Pro Val His Trp Val Gly Gln Ala Pro
41 ←-----CDR1-----→ 60

181 240
gga aaa ggg ctt gag tgg gta agt ttt gat cct gaa agt gga gaa tca atc tac gca
Gly Lys Gly Leu Glu Trp Val Gly Ser Phe Asp Pro Glu Ser Gly Glu Ser Ile Tyr Ala
61 ←-----CDR2-----→ 80

241 300
cgg gag ttc cag ggc agc gtc acc atg acc gcg gac aca tct aca gac ata gcc tac atg
Arg Glu Phe Gln Gly Ser Val Thr Met Thr Ala Asp Thr Ser Thr Asp Ile Ala Tyr Met
81-----→ 100

301 360
gag ctg agc agc ctg aga tct gac gac acg gcc gtg tat tac tgt gca gtc cct gac cct
Glu Leu Ser Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Val Pro Asp Pro
101 ←-----CDR3---→ 120

361 420
gat gct ttt gat atc tgg ggc caa ggg aca atg gtc acc gtc tct tca gcc tcc acc aag
Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys
121-----→ 140

421 450
ggc cca tcg gtc ttc ccc ctg gga tcc cgt
Gly Pro Ser Val Phe Pro Leu Gly Ser Arg
141 150

FIGURE 10

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VL BO 2C11

1 60
atg gaa acc cca gct cag ctt ctc ttc ctc ctg cta ctc tgg ctc cca gat acc acc gga
Met Glu Thr Pro Ala Gln Leu Leu Phe Leu Leu Leu Trp Leu Pro Asp Thr Thr Gly
1 20

61 120
gaa att gcg ttg acg cag tct cca ggc acc ctg tct ttg tct cca ggg gaa aga gcc acc
Glu Ile Ala Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
21 40

121 180
ctc tcc tgc agg gcc agt cag agt ttt agc agc tac tta gcc tgg tat cag cag aaa
Leu Ser Cys Arg Ala Ser Gln Ser Phe Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys
41 ←-----CDR1-----→ 60

181 240
cct ggc cag gct ccc agg ctc ctc atc tat ggt gca tcc acc agg gcc act ggc atc cca
Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro
61 ←-----CDR2-----→ 80

241 300
gac agg ttc agt ggc agt ggg tct ggg aca gac ttc act ctc acc atc agc aga ctg gag
Asp Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
81 100

301 360
cct gaa gat ttt gca gtg tat tac tgt cag aag tat ggt acg tca gcg atc acc ttc ggg
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Lys Tyr Gly Thr Ser Ala Ile Thr Phe Gly
101 ←-----CDR3-----→ 120

361 420
caa ggg aca cga ctg gag att aaa gga act gtg gct gca cca tct gtc ttc atc ttc ccg
Gln Gly Thr Arg Leu Glu Ile Lys Gly Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
121 140

421 426
cca tct
Pro Ser
141 142

Figure 11

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VH KRIX -1

1 60
atg gac tgg acc tgg agg atc ctc ttc ttg gtg gca gca gca gca gca gca cac tcc cag
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly Ala His Ser Gln
1 20

61 120
gtg caa ctg gtg caa tct ggg gct gag gtg aag aag cct ggg gcc tca gtg aag gtc tcc
Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
21 40

121 180
tgc aag acc tct gga tac aac ttc acc ggc tac tct gct tct gga cat atc ttc acc gcc
Cys Lys Thr Ser Gly Tyr Asn Phe Thr Gly Tyr Ser Ala Ser Gly His Ile Phe Thr Ala
41 ←-----CDR1-----60

181 240
tac tct gtg cac tgg gtg cga cag gcc cct gga caa ggg ctt gag tgg atg gga agg atc
Tyr Ser Val His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Arg Ile
61-----→ ←-----80

241 300
aac cct aac agt ggt gcc aca gac tat gca cat aaa ttt cag ggc agg gtc acc atg tcc
Asn Pro Asn Ser Gly Ala Thr Asp Tyr Ala His Lys Phe Gln Gly Arg Val Thr Met Ser
81-----CDR2-----→ 100

301 360
agg gac acg tcc atc agc aca gcc tac atg gaa ctg agc agg ctg aca tct gac gac acg
Arg Asp Thr Ser Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Thr Ser Asp Asp Thr
101 120

361 420
gcc atg tat tac tgt gcg aga gcc gac aac tat ttc gat att gtg act ggc tat act tct
Ala Met Tyr Tyr Cys Ala Arg Ala Asp Asn Tyr Phe Asp Ile Val Thr Gly Tyr Thr Ser
121 ←-----CDR3-----140

421 468
cat tac ttt gac tac tgg ggc cgg gga acc ctg gtc acc gtc tcc tca
His Tyr Phe Asp Tyr Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
141-----→ 156

Figure 12

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VL KRIX 1

1 60
atg gaa acc cca gct cag ctt ctc ttc ctc ctg cta ctc tgg ctc cca gat acc acc gga
Met Glu Thr Pro Ala Gln Leu Leu Phe Leu Leu Leu Trp Leu Pro Asp Thr Thr Gly
1 20

61 120
gaa att gtg ttg acg cag ttc cca ggc acc ctg tct ttg tct cca ggg gaa aga gcc acc
Glu Ile Val Leu Thr Gln Phe Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
21 40

121 180
ctc tcc tgc agg gcc agt cag agt gtt gcc agc gcc tac tta gcc tgg tac cag caa aaa
Leu Ser Cys Arg Ala Ser Gln Ser Val Ala Ser Ala Tyr Leu Ala Trp Tyr Gln Gln Lys
41 ←-----CDR1-----→ 60

181 240
cct ggc cag gct ccc agg ctc ctc atc tat ggt gca tcc agt agg gcc acc gac atc cca
Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Asp Ile Pro
61 ←----- CDR2-----→ 80

241 300
cac agg ttc agt ggc agt ggg tct ggg aca gac ttc act ctc acc atc agc aga ctg gag
His Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
81 100

301 360
cct gaa gat ttt gca gtg tac tac tgt cag caa tat ggt acc tca gcc tta ctc act ttc
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Thr Ser Ala Leu Leu Thr Phe
101 ←----- CDR3-----→ 120

361 420
ggc gga ggg acc aag gtg gag atc aaa cga act gtg gct gca cca tct gtc ttc atc ttc
Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe
121 140

420 429
ccg cca tct
Pro Pro Ser
141 143

Figure 13